REMARKS

Applicants take this opportunity to thank Examiner Anderson for the in-person interview conducted with applicants' representative on November 27, 2007.

Upon entry of the above amendment, claims 1-7, 15-23 and 42 will be pending in the present application. Applicants respectfully submit that neither the claim amendments nor the new claim add any new matter within the meaning of 35 USC §132. Accordingly, entry of these amendments is respectfully requested.

1. Rejection of claim 17 under 35 U.S.C. §112, 2nd paragraph as being indefinite

The Examiner states that the limitation "said surfactant" recited in claim 17 lacks sufficient antecedent basis. Presently pending claim 3 recites the surfactant limitation. Applicants respectfully note that claim 17 has been amended to be dependent upon claim 3. Because this claim has been amended to change the dependency, applicant respectfully requests that the Examiner reconsider and withdraw this rejection of pending claim 17.

2. Rejection of claims 1-8, 14-16 and 18-23 under 35 U.S.C. §103(a)

The Official Action states that claims 1-8, 14-16 and 18-23 are rejected under 35 U.S.C. §103(a) as being unpatentable over over Gilis *et al.* (WO 00/03697) and Ishibashi *et al.* (U.S. Patent Application No. 2003/0012815) in view of Mathir *et al.* (Journal of Microencapsulation, 1997).

As the basis for this rejection, the Official Action states in relevant part:

> Gilis *et al.* and Ishibashi *et al.* in view of Mathir *et al.* …provide the teaching, suggestion and motivation to use any suitable solvent system in order to provide a working solution for coating core particles.

Response

Applicant respectfully traverses this rejection of claims 1-8, 14-16 and 18-23. The cited references do not establish a *prima facie* case of obviousness against the presently pending claims.

To establish a prima facie case of obviousness, the PTO must satisfy three requirements. First, as the U.S. Supreme Court recently held in KSR International Co. v. Teleflex Inc. et al., Slip Opinion No. 04-1350, 550 U.S. (April 30, 2007), "a court must ask whether the improvement is more than the predictable use of prior art elements according to their

established functions. ...it [may] be necessary for a court to look to interrelated teachings of multiple patents; the effects of demands known to the design community or present in the marketplace; and the background knowledge possessed by a person having ordinary skill in the art, all in order to determine whether there was an apparent reason to combine the known elements in the fashion claimed by the patent at issue. ...it can be important to identify a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does... because inventions in most, if not all, instances rely upon building blocks long since uncovered, and claimed discoveries almost of necessity will be combinations of what, in some sense, is already known." (KSR, supra, slip opinion at 13-15). Second, the proposed modification of the prior art must have had a reasonable expectation of success, determined from the vantage point of the skilled artisan at the time the invention was made. Amgen Inc. v. Chugai Pharm. Co., 18 USPQ 1016, 1023 (C.C.P.A 1970). Lastly, the prior art references must teach or suggest all the limitations of the claims. In re Wilson, 165 USPQ 494, 496 (C.C.P.A. 1970).

A. Presently claimed subject matter

The present pending claims as exemplified by currently amended independent claim 1 are directed to:

> A method of manufacturing a water-insoluble azole antifungal active agent—oral dosage form, said method comprising the steps of: providing a single phase working solution comprising a water-insoluble azole antifungal active agent, water, a water-soluble polymer and a solvent, said solvent selected from the group consisting of alcohol, acetone, and mixtures thereof; providing core particles formed from a pharmaceutically acceptable material; combining said working solution with said particles to produce a water-insoluble azole antifungal active agent-coated particles; drying said water-insoluble azole antifungal active agent -coated particles; and forming said dried particles into an oral dosage form.

B. The Teachings of the Gilis *et al.* reference (WO 00/03697)

The Gilis *et al.* reference teaches pellets having a core coated with an antifungal and a polymer. The pharmaceutical dosage form disclosed in the Gilis *et al.* reference is prepared using a suitable solvent system comprising a mixture of dichloromethane and an alcohol. The Gilis *et al.* reference specifically teaches that the solvent mixture should comprise at least 50% by weight of dichloromethane (see p. 9, lines 17-20). Further, the Gilis *et al.* reference does not disclose a working solution containing both the drug and water, as required by the present claims.

C. The Teachings of the Ishibashi *et al.* reference (U.S. Patent Application No. 2003/0012815)

The Ishibashi *et al.* reference discloses a sustained release formulation prepared by spray-coating a solution containing a hydrophobic organic substance-water-soluble polymer mixture onto a drug-containing core substance, followed by spray-coating a different hydrophobic organic compound-water-soluble polymer mixture onto the resulting coating layer. The Ishibashi *et al.* reference teaches compositions formed by spraying a polymeric layer on top of a drug-containing core. This is different from the presently claimed process, which requires both the drug and the polymer in the same layer.

D. The Teachings of the Mathir *et al.* reference (Journal of Microencapsulation, 1997)

The Mathir *et al.* reference teaches the use of aqueous coating systems in controlled release drug dosage formulations as an alternative to organic-based coating systems. Chlorpheniramine maleate is disclosed as a highly water soluble drug whose pharmacokinetic profile is greatly improved by slowing its release into the body. Further, Mathir *et al.* teaches the use of chlorpheniramine maleate dissolved in ethanol

only, which is different from the working solution containing both the drug and water, as required by the presently pending claims.

E. The combination of references does not show all the elements of the pending claims, and thus cannot render these claims obvious

The presently pending claims are distinguishable from the cited references. None of the references, taken alone or in combination, contain all the elements of the presently pending claims, and thus cannot render these claims obvious. In particular, independent claim 1 recites a single phase working solution comprising a water-insoluble azole antifungal active agent, water, a water-soluble polymer and a solvent, said solvent selected from the group consisting of alcohol, acetone and mixtures thereof (Emphasis added).

In contrast, Gilis *et al.* and Ishibashi *et al.* both disclose dichloromethane as a suitable solvent. Accordingly, the solvent system recited in the present application is different from the solvent systems disclosed in the Gilis *et al.* and Ishibashi *et al.* references. The Gilis *et al.* reference does disclose that dichloromethane levels should be limited, however, the reference teaches away by including 50% dichloromethane in the solvent system. Nothing in the Gilis *et*

al. reference suggests a solvent system that does not include dichloromethane. Further, the Gilis *et al.* reference teaches that azole antifungal compounds are sparingly soluble in water, and that other non-aqueous based systems must be used in order to solubilize the compounds (see p. 1, lines 9-34).

The Ishibashi *et al.* reference teaches that solvents should be selected according to the hydrophobic organic compound and water soluble polymer used. However, the Ishibashi *et al.* reference discloses the use of dichloromethane and carbon tetrachloride as suitable solvents, which are specifically excluded from the presently pending claims. Further, the Ishibashi *et al.* reference does not state how to reduce or eliminate the levels of dichloromethane to the extent taught by the present application. Therefore, the Ishibashi *et al.* reference does not remedy the deficiencies of the Gilis *et al.* reference.

Regarding the Mathir *et al.* reference, this reference teaches the use of chlorpheniramine maleate dissolved in ethanol only, while the presently pending independent claim 1 teaches a working solution comprising a water-insoluble azole antifungal active agent, water, a water soluble polymer and a solvent, said

solvent selected from the group consisting of alcohol, acetone, and mixtures thereof.

Further, as discussed and agreed to by the Examiner during the interview on November 27, 2007, none of the cited references disclose a working solution containing the drug and water, as required by the present claims. Therefore, it would have been unexpected for a person having ordinary skill in the art to use water as a solvent for a water-insoluble drug. Further, Ishibashi *et al.* and Mathir *et al.* both teach compositions formed by spraying a polymeric layer on top of a core substance containing a drug. In contrast, the presently claimed process requires both the drug and the polymer to be contained in the same layer.

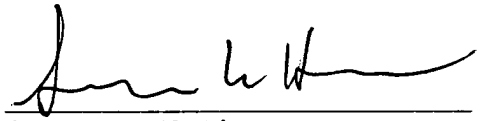
Accordingly, the Gilis *et al.*, Ishibashi *et al.* and Mathir *et al.* references, taken alone or in combination, do not show all of the elements of the presently pending claims, and thus cannot render these claims obvious.

Accordingly, Applicants respectfully request the Examiner to reconsider and withdraw the current rejection to presently pending claims 1-8, 14-16 and 18-23.

CONCLUSION

In view of the foregoing, applicants respectfully request the Examiner to withdraw the pending rejections and allow all pending claims 1-8, 15-23 and 42 to proceed to grant. If the Examiner has any questions or wishes to discuss this matter, she is welcomed to telephone the undersigned attorney.

Respectfully submitted,
THE NATH LAW GROUP

By: 

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